REMARKS

The Office action dated December 11, 2007 is acknowledged. Claims 1-6, 8-10, 12, 13 and 16-18 are pending in the instant application. According to the Office action, each of claims 1-6, 8-10, 12, 13 and 16-18 has been rejected. By the present Office Action response, claim 1 has been amended to incorporate the limitation of claim 9, claim 9 has been canceled and claim 18 has been amended to better define the claimed subject matter, support for which may be found in present claim 1. Reconsideration of the present rejection is respectfully requested in light of the amendments being made hereby and the arguments made herein. No new matter has been added.

Claim Objections

The Examiner has objected to claims 14 and 15 as being "use" claims. Claims 14 and 15 have been canceled. Therefore, this objection is no longer germane. Withdrawal thereof is respectfully requested.

Rejection of Claims 1-3 Under 35 U.S.C. 102(b)

Claims 1-3 have been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,759,445 (Yamamoto, et al.) as set forth in the Office action (pages 3-4). In particular, according to the Examiner, Yamamoto, et al. teach each and every feature of the present invention set forth in claims 1-3. Specifically, the Examiner states that Yamamoto, et al. disclose an aqueous dispersed solution, which comprises the steps of evaporating an organic solvent from a mixture prepared by adding cholesterol, lecithin, a surfactant and a neutral lipid, and/or a cholesterol ester in the organic solvent in a specific range of the concentration ratio. The Examiner also states that the references discloses the use of sodium cholate as the bile salt and tristearin (a type of triglyceride) which is

considered a nutrient and sodium as the ionic compound. The Examiner also notes that the sulfur compound need not be present in the prior art since it is optional in claim 1.

The Examiner states that Yamamoto, et al. fail to disclose the use of a composition for transdermal administration. However, the Examiner states that it does disclose the use of a composition as a standard solution for determining lipid levels. The Examiner further states that a statement of usefulness or contemplated use of a claimed compound or composition is usually given little weight in distinguishing it over the prior art. Thus, the Examiner concludes that Yamamoto, et al. disclose the invention as substantially claimed, and therefore anticipates, claims 1-3.

The Applicants respectfully disagree with the Examiner's conclusion and submit that the present invention is patentably distinct from the invention disclosed in the Yamamoto, et al. reference. Moreover, the Applicants submit that each and every feature set forth in claims 1-3 is not taught or disclosed by the cited reference, and therefore the reference does not anticipate the present invention as set forth in claims 1-3.

Yamamoto et al. teach a lipid-dispersed aqueous solution as a standard solution for determining the content of lipids, and a process for producing the same (col. 1, lines 7-9). According to example 1 (col. 2, line 65 – col. 3, line 36), 90 mg of phosphatidyl choline, 60 mg of cholesterol, and 4.5 mg sodium cholate as bile acid salt were dissolved in 2-propanol as an organic solvent. The organic solvent was evaporated, and water as an aqueous solvent was added to form dispersed lipid particles. Hence, this emulsion contains lecithins, bile acid salts and cholesterol in a ratio of 20:1:13.3. The ratios of the emulsions according to examples 2 and 3, which contain lecithins, bile acid (salt) and cholesterol, are 20:1:3.3 (90 mg of phosphatidyl choline, 15 mg cholesterol, and 4.5 mg

of deoxycholic acid or sodium taurodeoxycholate). Therefore, none of the examples of Yamamoto, et al. teaches a non-oily emulsion of lecithins, bile salts and cholesterol in a ratio of 2:1:1 as presently claimed.

Turning away from the examples toward the summary of the invention of Yamamoto, et al., it is disclosed by Yamamoto, et al. that the weight ratio from lecithin to cholesterol is from 1:1 to 4:1, and the weight ration of lecithin to bile acid salt is from 1:1 to 20:1 (col. 2, lines 38-41). Thus, Yamamoto, et al. teach weight ratios of 1:1:1, 4:4:1, and 20:1:20 (lecithins : bile salts : cholesterol), but fails to teach a ratio of these compounds as specified in present claim 1 (as amended), i.e. 2:1:1. The ratios as disclosed by Yamamoto, et al. do not consider that the amount lecithins exceeds the amounts of both other compounds (bile acid salts and cholesterol).

The Applicant thus respectfully submits that Yamamoto et al. fails to teach each and every limitation of present claim 1, and therefore does not anticipate the present invention as defined by present claims 1-3. Therefore, withdrawal of the present rejection is respectfully requested.

Rejection of Claims 1-6 and 8-10, 12, 13 and 16-18 Under 35 U.S.C. 103(a)

Claims 1-6 and 8-10, 12, 13 and 16-18 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto, et al. taken with Guo, et al. (Drug. Deliv. Vol. 7, No. 2, pp. 113-116, 2000)), Thorand, et al. (Southeast Asian J. Trop. Med. Public Health, Vol. 24, No. 4, pp. 624-630, 1993) and U.S. Patent No. 6,183,758 (Scott).

The Examiner states that the primary reference of Yamamoto, et al. discloses the presently claimed invention, as discussed above, but fails to teach the use of transdermal administration, use of non-oily emulsion which is a mixture of lecithin, bile salt and

cholesterol with the specific ratio and the amount disclosed in the present claims. However, the Examiner argues that the three cited secondary references make up for the deficiencies of Yamamoto, et al. and that it would have been obvious to combine the teachings of these references in order to arrive at the presently claimed invention.

The Applicant respectfully submits that to establish a *prima facie* case of obviousness, three basic criteria must be met, as set forth in M.P.E.P. § 2142. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The Applicant respectfully strongly disagrees with the Examiner's conclusion set forth in the Office action. In particular, the Applicant strongly asserts that the combination of the teachings of the secondary references fail to make up for the various deficiencies of Yamamoto, et al., as discussed above. The position of the Applicant will be discussed in greater detail below.

Regarding Guo, et al., the reference discloses transdermal delivery of insulin by using lecithin vesicles as a carrier, and investigates in vivo transdermal drug delivery by utilizing different lecithin vesicles. The references demonstrates that flexible vesicles with sodium cholate enable transdermal insulin delivery (Fig. 3), whereas conventional insulin-containing vesicles without sodium cholate, which are considered to be rigid vesicles, only have a minute effect on blood glucose concentration of treated mice (no hypoglycemic effect, see Fig. 3). Thus, rigid vesicles do not enable transdermal insulin administration.

Notably, Guo, et al. prepared the lecithin vesicles without cholesterol. Therefore, regarding the alleged obviousness of the presently claimed invention, it is submitted that one skilled in the art would not have considered incorporation of cholesterol into the flexible vesicles of Guo, et al. for transdermal administration of at least insulin, or if the emulsion disclosed by Yamamoto et al. would be suitable for transdermal insulin administration, if said emulsion would be loaded with insulin. It is known that the presence of cholesterol in a lipid membrane reduces membrane fluidity, and hence increases rigidity of the membrane. Based to the results of Guo, et al., it is submitted that a skilled artisan would refrain from considering rigid vesicles as suitable for transdermal administration of insulin and other drugs. Since cholesterol would be expected to increase rigidity of vesicles if it would be employed, a skilled artisan would thus refrain from utilizing cholesterol for preparing insulin-containing vesicles for transdermal delivery of said insulin, and would consider the emulsion as disclosed by Guo, et al. to be unsuitable since the emulsion comprises cholesterol.

The Applicant submits that the disclosures of Yamamoto, et al. and Guo, et al. might make obvious for a skilled artisan to use an emulsion of posphatidyl choline and sodium cholate for transdermal administration of insulin (or another polypeptide), but one skilled in the art would definitely refrain from employing cholesterol, as discussed above. Therefore, it is the Applicant's position that the combined teachings of Yamamoto, et al. and Guo, et al. teachings fail to make the subject matter of present claim 1, as amended, obvious to the skilled artisan.

Scott teaches that the combination of MSM and urea with propylene glycol and a medication provides a composition for administering said medication through the skin. Upon a thorough review of the disclosure of Scott, it is submitted that one has to acknowledge that MSM is always to be combined with urea in order to obtain some penetration of drugs through the skin. In this regard, the Applicant refers to col. 1, lines 51 to 60, col. 2, lines15 to 18; col. 3, lines 6 to 16; col. 3, line 22; col. 3, lines 32 to 34; col. 4, lines 3 to 5; claims 1, 2 and 6. Clearly, Scott does not teach that MSM can be used without urea. Moreover, Scott teaches that the combination of MSM and urea is to be combined with propylene glycol for transdermal administration of a medication.

Although an organic sulfur compound is an optional component of the composition of the present invention, the language of the present claims neither considers nor allows the presence of urea and/or propylene glycol in the composition of the present invention. However, Scott does not indicate that MSM alone, without urea and propylene glycol, would provide an efficient permeation enhancing agent. Thus, it is submitted that one skilled in the art would conclude form the combination of Yamamoto, et al. and Scott that an organic sulfur compound may become a component of the composition for transdermal drug delivery, if urea or urea and propylene glycol is added as well (as taught by Scott). Therefore, the teachings of the Scott reference fail to render the presently claimed invention, namely, the use of an organic sulfur compound alone, obvious did not make obvious.

Moreover, the disclosures of Yamamoto, et al., Guo, et al., and Scott have to be combined with respect to the claimed embodiment comprising an organic sulfur compound. In this regard, it is submitted that the combined view of these three

references may make a composition for transdermal insulin administration obvious to the skilled artisan that lacks cholesterol, but contains urea and propylene glycol. Contrary to what might have been obvious to the skilled artisan, the claimed composition contains a considerable amount of cholesterol, but does not comprise urea or propylene glycol. Hence, the claimed composition is clearly not rendered obvious.

With respect to the reference of Thorand et al., the Applicant submits that said reference may teach that administration of iron is effective in treating anemia. However, pursuant to Thorand, et al.'s disclosure, the iron is administered by tablets, i.e. via oral application. The Thorand, et al. reference does not provide any information that would indicate that the iron compound can be administered transdermally as well, nor does the Thorand, et al. reference provide any technical information that would enable the skilled artisan to provide a composition that allows efficient transdermal iron administration. Although it is feasible that Thorand, et al. may provide an object that is also an object of the present invention, i.e. looking for routes of administering iron in order to treat anemia. However, Thorand, et al. do not provide any technical solutions that would lead the skilled artisan towards the presently claimed invention. Therefore, the Applicant submits that the combination of Yamamoto, et al, with Guo, et al. and Thorand, et al. fails to render the embodiment of the present invention pertaining to a composition for transdermal administration of iron or another nutrient obvious.

In view of the above, it is therefore respectfully submitted that the present invention defined in the presently amended claims is patentably distinguishable over the combination of prior art teachings under 35 U.S.C. 103(a). Based on the aforementioned differences, each and every element of the present invention recited in the present claims

are not set forth in Yamamoto, et al., alone or in combination with any of the cited secondary references. Moreover, one skilled in the art would not be motivated to combine the teachings of said references or to modify Yamamoto, et al. to arrive at the presently claimed invention. Even if one were to do so, there would be no expectation of success. Therefore, the Applicant respectfully requests that this rejection be withdrawn.

Conclusion

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments, amendments to the claims and deficiencies of the prior art references, the Applicant strongly urges that the obviousness-type rejection and anticipation rejection be withdrawn. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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